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| APPLICATION NO.                             | FILING DATE | FIRST NAMED INVENTOR  | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|-----------------------|---------------------|------------------|
| 09/811,162                                  | 03/16/2001  | Manuela Martins-Green | 407E-000500US       | 5788             |
| 22798                                       | 7590        | 06/28/2004            | EXAMINER            |                  |
| QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C. |             |                       | DEBERRY, REGINA M   |                  |
| P O BOX 458                                 |             |                       | ART UNIT            | PAPER NUMBER     |
| ALAMEDA, CA 94501                           |             |                       | 1647                |                  |

DATE MAILED: 06/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/811,162

**Applicant(s)**

MARTINS-GREEN ET AL.

**Examiner**

Regina M. DeBerry

**Art Unit**

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 25 March 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 7,8,88,90,92,93,97,98 and 100-103 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 7,8,88,90,92,93,97,98 and 100-103 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

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***Status of Application, Amendments and/or Claims***

The amendment filed 25 March 2004 has been entered in full. Claims 1-6, 9-87, 89, 91, 94-96, 99 were cancelled. New claims 102 and 103 were added.

Claims 7, 8, 88, 90, 92, 93, 97, 98, 100-103 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Withdrawn Objections And/Or Rejections***

The rejection of claims 6-8, 88, 90, 92, 95, 97, 98, 100 and 101 under 35 U.S.C. 102(b) as being anticipated by Stern *et al.*, US Patent No. 5,641,867, as set forth at pages 6-8 of the previous Office Action (21 October 2003) is *withdrawn* in view of the amendment (25 March 2004).

**Claim Rejections - 35 USC § 112, First Paragraph, Written Description (New Matter)**

Claims 7, 8, 92, 93, 97, 98, 100-103 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is set forth at pages 2-3 of the previous Office Action (21 October 2003).

Applicant argues that from the teaching that exemplary fragments can range from about 5 to about 50 amino acids in length, one skilled in the art understands that

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exemplary fragments can be 5, 6, 7, and so on, up to 50 amino acids in length, although one also understands that other lengths are possible, so long as the fragment includes a functional differentiation domain. Applicant maintains that the specification's disclosure that fragments could be longer does not negate the clear teaching that the fragments could be for example 5, 6, 7, or 8 amino acids in length. Applicant submits that the specification clearly conveys to those of ordinary skill in the art that Applicant invented the polypeptide of claim 7, which is no greater than about 8 amino acids in length.

Applicant argues that the fact that the specification contemplates other embodiments is irrelevant to the question of whether the embodiment now recited in claim 8, wherein the IL-8 fragment is no greater than about 15 amino acids in length is adequately supported in the specification. Applicant cites more case law. Applicant argues that the specification described a genus of about 5 to about 50 amino acids in length, with subgenuses of about 8 to about 25 and about 8 to about 15 and specific examples of 6 and 11 amino acids in length. Applicant argues that the notion that the disclosure fails to satisfy 112, first paragraph rejection with respect to the recitations, in claims 7 and 8 of "not greater than about 8" or "not greater than about 15" can only result from a hypertechnical application of legalistic prose relating to that provision of the statute.

Applicant's arguments have been fully considered but not deemed persuasive. As Applicant has submitted, the specification states, "the chemokine fragment must be large enough to include a functional differentiation domain." "Chemokine fragments

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useful in the invention, can, for example, range from about 5 to about 50 amino acids in length, although other lengths are possible". "Preferred fragments range from about 8 to about 25 amino acids, and more preferably from about 8 to about 15 amino acids in length" (page 26, lines 26-31). The limitation, "from about 8 to about 15 amino acids in length", encompasses 8 amino acids in length and 15 amino acids in length. However, having the claims recite "no greater than about 8 amino acids in length" or "no greater than about 15 amino acids in length" is new matter because it excludes 9, 10, 11, 12, 13, 14 and 16-50 amino acid lengths contemplated in the specification *as originally filed*. The original limitation "from about 8 to about 15 amino acids in length" contemplates that the fragment may have more than 8 amino acids (or less) or more than 15 amino acids (or less). By changing the limitation **to explicitly recite** "no greater than about 8 amino acids in length" or "no greater than about 15 amino acids in length", Applicant has eliminated the upper limit of amino acid lengths, **which was not originally excluded**, resulting in newly changing the scope of disclosure and the scope of that which was contemplated at the time of filing and resulting in new matter.

Adding the expressed exclusion of certain elements implies the permissible inclusion of all other elements not so expressly excluded. This clearly illustrates that such negative limitations do, in fact, introduce new concepts (Ex parte Grasselli, 231 USPQ 393 (BPAI 1983)). It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads (MPEP 2163.05 Changes to the Scope of Claims). The evidence as whole indicates that the rejection should be maintained.

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**Claim Rejections - 35 USC § 112, First Paragraph, Enablement**

Claims 7, 8, 88, 90, 92, 100, 101, 103 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The newly amended claims encompass polypeptides comprising IL-8 fragments which are cyclic. The specification fails to teach or provide working examples, which demonstrate that IL-8 cyclic fragment peptides stimulate differentiation of fibroblasts to myofibroblasts. The level of unpredictability is high, because one skilled in the art cannot readily anticipate the effects of the biological activity of cyclic IL-8 peptides versus its linear counterpart. Furthermore, the art suggests that regions directly involved in binding and in providing the correct three-dimensional spatial orientation of binding and active sites are critical to protein's structure, function relationship. The Examiner has cited Ngo *et al.* to demonstrate this (Ngo *et al.*, 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 433-440 and 492-495).

IL-8 is a chemokine which has specific activity upon binding its receptor. The specification fails to consider the dynamics of protein folding and the effect of receptor binding. The specification has provided no guidance to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (changes necessary for cyclization of fragments), the correct three-dimensional spatial orientation of binding/active sites and the nature and extent of

changes that can be made in these positions to make functioning IL-8 cyclic fragment peptides.

Due to the large quantity of experimentation necessary to determine the positions in IL-8 fragments which are tolerant to change, the correct three-dimensional spatial orientation of binding/active sites and the nature and extent of changes that can be made in these positions to make IL-8 cyclic fragment peptides and screen same for the activity of differentiation of fibroblasts to myofibroblasts, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention and the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, undue experimentation would be required of the skilled artisan to make and/or use the claimed persuasive.

### **Claim Objection**

Claims 102 and 103 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claim 102 recites the limitation, "about 5 or more amino acids in length" but depends from claim 7, which recites the limitation, "no greater than about 8 amino acids in length". Claim 103 recites the limitation, "about 5 or more amino acids in length" but depends from claim 8 which recites the limitation, "no greater than about 15 amino acids in length". Claims 102 and 103 fail to further limit the subject matter of the previous

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claims because the claims encompass "greater than 8 amino acids in length" and "greater than 15 amino acids in length" respectively.

Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

### ***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.



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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



RMD  
6/23/04



ELIZABETH KEMMERER  
PRIMARY EXAMINER